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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,864	06/28/2001	Kciichi Yokoyama	209524US0 CONT	3226

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EXAMINER	
PATTERSON, CHARLES L JR	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 06/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,864	YOKOYAMA ET AL.	
	Examiner	Art Unit	
	Charles L. Patterson, Jr.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,12-38,41-43,72,73 and 75-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-9,12-37,76-78 and 85* is/are allowed.

6)☒ Claim(s) *38,41-43,72,73,75,79-84 and 86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 38, 41, 42, 72-73, 75, 79-84 and 86 are rejected under 35 U.S.C. 102(e) as being anticipated by Yokoyama, et al. (AA). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that Yokoyama, et al. do not teach an "intermediate state" as in claim 38. Applicants argue that the reference does not teach a transglutaminase that passes through a denatured state. The examiner does not agree. "Intermediate state" could refer to anything whatsoever that is intermediate between one state and another since it is not further defined in the claim. The enzyme does in fact pass through a denatured state, as in the recitation *supra*, but "intermediate state is not in any way limited to this

denatured state. In column 12, lines 50-67, it is taught that "MTG [microbial transglutaminase] inclusion bodies...was partially purified by repeating the centrifugation several times, and then dissolved in 8 M urea...to obtain the 2 mg/ml solution...and the solution was [then] diluted to a concentration of 0.5 M urea with 50 mM phosphate buffer (pH 5.5)...[and that the final] specific activity of the aspartic acid residues-lacking MTG was about 30 U/mg... [which is] equal to the specific activity of natural MTG". As to claim 75, it is maintained that the transglutaminase taught by the reference has the properties recited in the claim, absent proof to the contrary. The patent office does not have the facilities to assay enzymes as to properties and therefore once a *prima facie* case has been made by the examiner it is up to applicants to show that the requirements of claim 75 are not met by the instant reference.

Claims 38, 41-43 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ejima, et al. (AY). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that they have included the limitations of claim 11 in claim 1 and therefore the previous rejection over claims 1-10, 13-14, 18, 19 and 21-37 have been dropped. They then argue that regarding the claims indicated *supra* as still rejected, the instant reference describes the purification of hIL-6 and that this reference is not concerned with the purification of transglutaminase and that the specification teaches that "it is difficult to make predictions about the ability to refold a protein". They then argue that Ejima, et al. discloses in column 1, page 302 that "the native conformation of hIL-6 was obtained by rapidly removing the denaturant from the oxidi-

zed hIL-6 solution without any dilution" and that this suppressed aggregation during the refolding process, but that in the paragraph spanning columns 1 and 2 of page 302 it is stated that "The pellet of inclusion bodies was solubilized in 6M GdnHCl...Solubilized hIL-6 was rapidly diluted 10-fold...". They then state that "Applicants wonder how in the face of such contradictory teachings one of skill in the art would expect *any* results based on Ejima et al" (emphasis in original). To start with, the examiner stated in the last action that he had been unable to find the first recitation, but applicant did not further explain specifically where the instant recitation was. The applicant has re-examined column 1 and has finally found the cited recitation on lines 3-6. This statement is in the Introduction to the paper whereas the examiner cannot find anything in the rest of the paper stating that the there was no dilution. In fact the sentence spanning columns 1 and 2 of page 302 and the first sentence in column 2 on that page both state that the solution was "rapidly diluted 10-fold". Therefore it is maintained that one of ordinary skill in the art would take the entirety of the paper rather that one statement in the introduction as indicative of what is taught by the reference.

Claims 38, 41-43, 72-73, 79-81 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ejima, et al. (AY) in view of Yokoyama, et al. (AA). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that Yokoyama, et al. does not teach forming an intermediate structure. This is not what was relied on to add this reference to the instant rejection. As stated in the previous rejection, the reference is

relied on to teach that the use of transglutaminase to produce food and toiletries ("gelled cosmetics") is taught in column 1, lines 16-25 of Yokoyama, et al.

The previous 35 U.S.C. 103(a) rejection over Yokoyama, et al. (AA) is hereby dropped after considering applicants arguments concerning a concentration of 2/mg/ml vs. 10 mg/ml.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
June 3, 2004